AVERY'S "NEUROTIC RELUCTANCE"

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Stephen Toulmin pioneered a major advance in the philosophy of science when he demonstrated how examples from the history and present practice of science could be relevant to the philosopher's enterprise [1]. In his most recent major contribution, *Human Understanding,* Toulmin uses examples from the history of science to illustrate his central claim that science often advances through changes "in the very *criteria* of 'rationality' " [2]. The claim is a crucial one because, if true, it implies that, if science is rational at all, it is only "rational" in a much weaker sense than scientists have believed and philosophers have hoped.

The plausibility of Toulmin's claim rests heavily on the three examples he cites from the history of science. Each of them deserves careful attention, but here I will focus on the second: Oswald Avery's "almost neurotic reluctance" to identify DNA with genes.

Toulmin's one-page account [2] depends almost exclusively on a paper by *Perspectives in American History* editor Donald Fleming [3]. As a result, any criticism of Toulmin's page is even more a criticism of Fleming's paper. For Toulmin, however, the account assumes an importance that it never had for Fleming. In Fleming, the account is part of a survey of the effects of the emigration of German scientists due to the rise of the Nazis. In Toulmin, however, the account is central evidence for a crucial generalization about science, namely, that scientific criteria of rationality are not stable and universal.

By Toulmin's account, "biochemical questions about the material nature of the gene were unimportant, if not entirely irrelevant," to Avery and his colleagues because of "their commitment to the currently accepted attitudes of classical genetics." The result, according to Toulmin, was that Avery's classic 1944 paper was, in Fleming's words, "muffled and circumspect." Avery and his coauthors were (here Toulmin again

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quotes Fleming) " 'almost neurotically reluctant' to identify genes with DNA" [2]. What made advance in biology possible was the entry into the field of the new physicist-biologists such as Astbury, Delbruck, and Szilard. These men held different criteria of rationality in science, for they, unlike Avery and his colleagues, valued "a radical physical explanation" of biological phenomena [2].

Such is the account of Toulmin's second example. If the account is accurate, then the example seems to provide good evidence of the changeability of the criteria of scientific rationality. The question is whether the account is accurate. In the remainder of this note, two grounds for doubting the accuracy of the account will be explored: (1) that Avery's reluctance has been exaggerated and (2) that to the extent that the reluctance existed, it arose from criteria Avery shared with the physicist-biologists.

Toulmin, quoting Fleming [3, p. 152], claims that Avery was "almost neurotically reluctant to identify genes with DNA." As evidence for the claim, Fleming quotes a sentence from Avery in which he admitted that substances other than DNA may possibly be involved in genetic transformation. But Fleming does not quote the following sentence in which Avery says, "If . . . the biologically active substance isolated in highly purified form as the sodium salt of deoxyribonucleic acid actually proves to be the transforming principle, as the available evidence strongly suggests, then nucleic acids of this type must be regarded not merely as structurally important but as functionally active in determining the biochemical activities and specific characteristics of pneumococcal cells" [4].

This statement hardly shows "neurotic reluctance," especially when considered in the light of the good reasons Avery had for qualifying his claim. Further, if there was, in fact, such reluctance, we would expect it to be reflected in Avery's private correspondence either as resistance to the identification of DNA with genes or at least as depression at the necessity of making such an identification. On the contrary, when he writes to his brother, Avery is delighted at the possibility that DNA is the genetic material: "If we are right, and of course that is not yet proven, then it means that nucleic acids are not merely structurally important but functionally active substances in determining the biochemical activities and specific characteristics of cells and that by means of a known chemical substance it is possible to induce predictable and hereditary changes in cells. This is something that has long been the dream of geneticists" [5]. Once again, whatever reluctance Avery had was based, not on his resistance to DNA being genes, but rather to public prudence arising from limitations in the evidence: "It is lots of fun to blow bubbles but it is wiser to prick them yourself before someone else tries to" [5].

Finally, it should be noted that, according to Avery's coauthor McCarty [6, p. 187], some of the apparent reluctance in the paper is due to changes made by *Journal of Experimental Medicine* editor Rous. For example, a quotation from Leathes that DNA would one day surpass the proteins in importance was deleted by Rous as being merely speculative.

So far, I have shown that Avery's reluctance to identify DNA with genes has been exaggerated. Now I will argue that, to the extent that the reluctance existed, it arose from values shared with the physicist-biologists.

Several limitations in Avery's experiment justified public caution. The experiments had been done using just one type of bacteria, and difficulties had been encountered in inducing transformation in vitro. Also, as Hotchkiss claims, ". . . since at that time the operational unit—the sperm nucleus or viral particle—could not be broken down experimentally into injectable nucleic acids, then for Avery it seemed merely clever for him to do so only conceptually, and a rather vainglorious and irresponsible thing to do, before an impressionable public" [7, p. 6]. But the primary limitation in the experiment was the lack of certainty that all of the non-DNA material had been filtered out. At the time, the most likely candidate for being the genetic material was protein. Thus, there was no certainty in the conclusion that DNA was the genetic material, so long as there remained even minute traces of protein present in the experiment's transforming substance. Robert Olby has presented a persuasive critique of the position of the best known of the pro-protein advocates, Mirsky [8]. But by making Mirsky the main villain in the piece, Olby misleadingly leaves the impression that few shared Mirsky's doubts. Actually, at the time of the Avery paper, even the physicist-biologists were cautious in concluding that genes were made of DNA. Two years after the publication of the paper, a conference was held at Cold Spring Harbor, a center of activity for the physicist-biologists. Here McCarty presented the results of additional joint work with Avery. Attendee Bently Glass reports on the paper's reception [9, p. 107–108]:

> If my memory does not play me false, the reaction among geneticists was about as follows. The demonstration that the transforming principle is DNA is very strong, although purification is not so complete that everyone is convinced that some protein does not remain in the preparation. (Mirsky was not present and could not have been directly responsible for this opinion.) We must recognize, it was said, that only a single gene need be transferred to transform the rough cells to smooth, and the presence of a single protein gene in the partially purified material cannot be firmly excluded. Inasmuch as suspended judgment is considered to be a great scientific virtue, we should suspend judgment. Opposing this view was evidence presented in the paper by McCarty, Taylor and Avery (as well as in others by McCarty and by McCarty and Avery published in 1946), that deoxyribonuclease rapidly destroys the transforming principle, but that it is not

affected by protein denaturation or precipitation procedures or by action of proteases.

Speaking of the same period, no less a figure than James D. Watson reports that ". . . despite Avery, McCarthy [*sic*] and MacCleod, we were not at all sure that only the phage DNA carried genetic specificity" [10].

Thus, while it may be that the case of pre-DNA biology is a good case of scientists having different strategies due to their differing endowments of human capital and to their differing judgments of competing programmes, it does not seem justified to claim that this case reflects a change "in the very *criteria* of rationality" [2], nor does it seem to be a case where the profession failed to "share agreed—or sufficiently agreed—conceptions of 'explanation' " [2].

Although the physicist biologists did not differ from Avery, McCarty, and MacCleod in their criteria of rationality, the failure of this case to exemplify Toulmin's broader thesis does not in itself refute the thesis. Even if Avery and his colleagues, all of whom were medical bacteriologists, shared criteria with the physicist-biologists, nothing can be inferred about the criteria held by the classical geneticists. Indeed, McCarty has observed that "the classical geneticists of this period with rare exceptions were simply not interested in the chemical nature of genetic material" [11]. Although such disinterest might merely reflect pessimism about the likelihood of learning the chemical nature of the gene, it might also reflect different criteria about what constituted a good explanation in genetics. If so, then the larger story of DNA might still provide evidence for Toulmin's thesis, even though the particular episode involving Avery does not.

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A P♀ME—FER U♂

"I'm tired of bein' all RNA," she said.
Tired of being the disposable carbon
Paper for somebody else's charge-a-plate,
Whose magic logos is key to protean
Riches, to witch *another's* ancient runes
Scop Poiesis.

I'd like to No, Y, while you solemnly
Pronounce the ways of the world . . . why . . . I . . .
Keep cookin', and neatin' up, and dittoin'
Your memos. Well . . . You see, I don't
Transcribe well. I doodle with your vestiges.
Jiggle. Giggle.

Virginia Hansen